Noncompliance with Antihypertensive Medications
The Impact of Depressive Symptoms and Psychosocial Factors

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OBJECTIVE: **Addressing the epidemic of poor compliance with antihypertensive medications will require identifying factors associated with poor adherence, including modifiable psychosocial and behavioral characteristics of patients.**

DESIGN: **Cross-sectional study, comparing measured utilization of antihypertensive prescriptions with patients' responses to a structured interview.**

STUDY POPULATION: **Four hundred ninety-six treated hypertensive patients drawn from a large HMO and a VA medical center.**

DATA COLLECTION: **We developed a survey instrument to assess patients' psychosocial and behavioral characteristics, including health beliefs, knowledge, and social support regarding blood pressure medications, satisfaction with health care, depression symptom severity, alcohol consumption, tobacco use, and internal versus external locus of control. Other information collected included demographic and clinical characteristics and features of antihypertensive medication regimens. All prescriptions filled for antihypertensive medications were used to calculate actual adherence to prescribed regimens in a 365-day study period.**

MAIN OUTCOME OF INTEREST: **Adjusted odds ratios (ORs) of antihypertensive compliance, based on ordinal logistic regression models.**

RESULTS: **After adjusting for the potential confounding effects of demographic, clinical, and other psychosocial variables, we found that depression was significantly associated with noncompliance (adjusted OR per each point increase on a 14-point scale, 0.93; 95% confidence interval [95% CI], 0.87 to 0.99); in unadjusted analyses, the relationship did not reach statistical significance. There was also a trend toward improved compliance for patients perceiving that their health is controlled by external factors (adjusted OR per point increase, 1.14; 95% CI, 0.99 to 1.33). There was no association between compliance and knowledge of hypertension, health beliefs and behaviors, social supports, or satisfaction with care.**

CONCLUSIONS: **Depressive symptoms may be an under-recognized but modifiable risk factor for poor compliance with antihypertensive medications. Surprisingly, patient knowledge of hypertension, health beliefs, satisfaction with care, and other psychosocial variables did not appear to consistently affect adherence to prescribed regimens.**

KEY WORDS: **antihypertensive medication; adherence; depressive symptoms; psychosocial factors.**

Despite the availability of effective therapy, hypertension remains poorly controlled in the United States and other industrialized countries. In the Third National Health and Nutrition Examination Survey, nearly half of hypertensive patients in the community-based sample were found to be taking no prescription medication, and only one quarter of those who were being treated had their blood pressure adequately controlled.[1] Patient noncompliance with prescribed treatments is a central reason for the failure to control hypertension in those receiving therapy.[2] Numerous investigations have found that half of hypertensive patients do not comply adequately with treatment, and that half of those with "refractory" hypertension are in fact nonadherent.[3–7] Such high levels of noncompliance are of tremendous concern, given the serious consequences of uncontrolled hypertension on cardiovascular, cerebrovascular, and renal morbidity as well as mortality.[8]

Clearly, interventions to improve adherence with antihypertensive medications are needed. However, if such interventions are to be successfully designed, targeted, and cost-effective, it is critical to understand the complex reasons for nonadherence, and to identify those that are modifiable.[9] Investigators have identified some sociodemographic and clinical features associated with compliance (e.g., age, gender, race, education, employment, socioeconomic status, or the presence of specific comorbid conditions such as cardiovascular disease), although the findings are inconsistent.[2,3,10–16]

Despite the likelihood that psychosocial and behavioral characteristics may be important determinants of compliance, few rigorous studies have defined the impact of these features on adherence; those that have been conducted have produced inconsistent results. The variable receiving the most attention has been patients' health beliefs, including their perceptions of the threat posed by the condition, the effectiveness of treatments, and the importance of complying with therapy.[17–19] Other psychosocial variables thought to influence antihypertensive medication adherence include: knowledge of hypertension and its treatment[14,20]; social support[21,22]; satisfaction with health care[10,23,24]; and the locus of control (i.e., the degree to which a patient feels that control over their

circumstances is internal or external).[25] Behaviors that have been examined and related to compliance with blood pressure medication have included use of alcohol or substances[2,26] and smoking.[14] The effect of psychopathology on compliance with medications for other cardiovascular conditions has been considered, but rigorous study of such relationships has been limited.[27]

Unfortunately, few studies of the relationships between psychosocial factors and compliance with antihypertensives have been adequately powered, simultaneously adjusted for other determinants of compliance, or conducted in typical clinical populations; and few have used precise assessments of compliance. Therefore, in the current study, we employed typical outpatient populations and an objective measure of compliance to test the hypothesis that believing in the importance of treating hypertension, possessing greater knowledge, having more social support, being more satisfied, having a more external locus of control, responding in a more socially desirable manner, having fewer depressive symptoms, and consuming less alcohol or tobacco would all be associated with greater compliance with antihypertensive medications. Although our hypothesis was limited to the independent effects on compliance of these understudied psychosocial and behavioral variables, we also considered it essential to adjust for more established determinants including demographic, clinical, and health care utilization variables.

METHODS

Study Population

Participants in this study consisted of patients with diagnosed hypertension who received their care in 1 of 2 typical settings: a large HMO and a Veterans Affairs medical center (VAMC), both in the northeastern United States. The HMO is a long-established not-for-profit managed care organization caring for 350,000 members; during the study period it provided comprehensive drug coverage with a minimal co-payment. The VAMC was affiliated with the Brigham and Women's Hospital and Harvard Medical School and provided all patients with free prescription coverage.

In both settings, computer-based patient information systems captured all periods of enrollment, recorded diagnoses, physician visits, hospitalizations, and medication utilization. These systems were used to identify members who met all of the following inclusion criteria: 1) age $\geq$40; 2) filled a first (index) prescription for any antihypertensive medication during calendar year 1996; 3) had a diagnosis of hypertension recorded in their electronic records prior to filling their index antihypertensive prescription; and 4) were continuously enrolled during the 180 days prior to and 365 days following their index prescription. From this eligible group, a random sample of 513 HMO patients and 480 VAMC patients were mailed a letter inviting them to participate in the telephone survey.

These patients were given 2 opportunities to decline participation: first, by returning a postcard which had been mailed to them saying they did not wish to participate; and second, by declining when they were called by the research assistant conducting the telephone survey. Participation rates were 48% among HMO patients (248 of 513 invited) and 52% among VAMC patients (248 of 480 invited). Eligible subjects and participants did not differ in terms of their demographic characteristics at either site; we did find that participants were more likely than all eligible subjects to be taking β-blockers or ACE inhibitors at the VAMC site. The study design was approved by the institutional review boards of the Brigham and Women's Hospital and all other participating institutions.

Data Collection

The survey instrument used in this study was developed following extensive review of the literature and discussions with hypertensive patients and physicians caring for hypertensive patients. Tools to assess patient characteristics were either adapted from existing measures or newly developed (see below). The resulting instrument was pilot tested on non-study patients with hypertension prior to use to evaluate the understandability of survey questions and the feasibility of administering, by telephone, items that had been originally designed for pencil-and-paper or face-to-face administration. The final survey required approximately 45 minutes to administer. Three research assistants who conducted the telephone surveys were trained to ensure consistency and comparability of administration both across subjects and between research assistants.

Definition of Psychosocial and Behavioral Variables

Measures for use in the survey instrument were chosen based on the required time for assessment, the feasibility of administration by telephone and lay interviewers, the appropriateness of use in our study population, and known psychometric properties. Several measures were modified from their original form to decrease the amount of time required to complete the survey. All modifications to items are described below:

Depression Symptom Severity. The presence and severity of depressive symptoms in each respondent was assessed using items from the Brief Symptom Inventory depression subscale.[28] This consists of 7 items assessing the degree to which respondents experience depressed mood, loss of interest, vulnerability to criticism, loneliness, worthlessness, hopelessness, and thoughts of suicide. Our adaptation consisted of using 3 response categories ("hardly ever," "sometimes," or "often," scored 0, 1, or 2, respectively) instead of the original five, to create a total depression severity score ranging from 0 to 14. The criterion validity of this adapted scale was investigated by

comparing total scores with the likelihood of having a diagnosis of depression recorded in one's medical record.

Health Beliefs. Nine statements were taken from Norman et al.[19] concerning how important or beneficial it was to take medications for hypertension (e.g., taking blood pressure medications would lower the chances of heart disease; treating hypertension was more important relative to treating other medical conditions; taking blood pressure medications was only necessary during periods of feeling tense or nervous). Adaptations consisted of assigning a 1 or 0 to endorsing or not endorsing the statement, respectively (rather than using the original 5 response categories) to create a total belief score ranging from 0 to 9.

Knowledge Regarding Hypertension and Its Treatment. We selected 14 items from previous studies that assessed a respondent's knowledge of hypertension, including what normal systolic and diastolic pressure readings should be, sequelae of uncontrolled hypertension, and treatments for hypertension.[29,30] Our adaptations included assigning a 1 or 0 to responses indicative of having knowledge or not, respectively. Responses to all 14 items were summed to create a total knowledge score ranging from 0 to 14, with higher scores indicating greater knowledge.

Social Support Regarding Blood Pressure Medications. To assess the degree to which respondents were receiving social support to take their medications, we used 2 items from Norman et al.[19] that measure how much family or friends attempted to help the patient use blood pressure medicines properly. Items were adapted by assigning responses 0, 1, or 2, corresponding to "none," "somewhat," and "very much," respectively (instead of the original 4 response categories). Responses to both items were used to create a total social support score ranging from 0 to 4.

Internal Versus External Locus of Control. To measure the degree to which patients consider control over events to reside within (internal locus) or outside (external locus) themselves, we adapted a scale developed by Rotter by selecting 5 of 29 original pairs of statements.[31] Endorsing a statement indicative of possessing an external locus of control was assigned a 1 (e.g., "I usually don't have much influence over the things that happen to me.") while endorsing a statement indicative of an internal locus of control was assigned a 0 (e.g., "I don't think that chance or luck plays an important role in my life."). Responses from all pairs of statements were used to construct an external locus of control score ranging from 0 to 5.

Patient Satisfaction. We chose 5 items from prior investigations[10,23,24] that asked the degree to which respondents were satisfied with clinic waiting times, availability of the doctor, amount of time their doctor spent with them, amount of information received from their doctor, and concern their doctor had for the patient's health. Responses to each item were assigned 0, 1, or 2, corresponding to "not," "slightly," or "extremely satisfied," respectively, and used to calculate an overall satisfaction score ranging from 0 to 10.

Alcohol Consumption. Alcohol consumption was assessed with 3 questions asking for the quantity consumed and frequency of use of beer, wine, and liquor. A respondent's average number of drinks per day was calculated assuming an equivalency between 12 ounces of beer, 1 glass of wine, and 1 shot of liquor. A continuous measure of alcohol consumption was employed, rather than one designed to dichotomize subjects into those with likely alcoholism, to be able to investigate whether consumption of even modest amounts of alcohol could interfere with compliance behavior.

Tobacco Use. Because of the relatively small number of respondents who reported smoking, current tobacco consumption was represented as a dichotomous (yes/no) rather than continuous variable.

Socially Desirable Responding. Taking medications as ordered is a behavior with well-established societal norms, which could influence a subject's reported answers to an interviewer's questions. As a result, a response bias could occur if study participants were to respond to questions in a socially desirable manner rather than accurately. In turn, this could obscure or spuriously create associations between psychosocial/behavioral variables and antihypertensive medication compliance. To measure the degree to which subjects answered questions with "approved" responses, we adapted the Marlow-Crowne Scale by including a 10-item subset of the original instrument.[32] Responses to each item (e.g., "I never hesitate to go out of my way to help someone in trouble.") were assigned 1 if socially desirable (e.g., responding with "yes") and 0 if not (e.g., responding "no"). We used this instrument to create a socially desirable response score ranging from 0 to 10.

In the very rare instances in which subjects refused or were unable to answer items, we assigned them the lowest level of the characteristic inquired about (i.e., the lowest level of depression symptom severity, belief in the importance of treating hypertension, knowledge, social support, external locus of control, satisfaction, socially desirable responding, alcohol and tobacco consumption).

Assessment of Compliance

To calculate compliance, we analyzed the quantity dispensed and days' supply fields for each prescription for any antihypertensive medication that was filled by each subject during the 365-day period after their first recorded (index) prescription in 1996. This made it possible to develop a person-time calendar to indicate on which days during the 365 days following the index prescription each

patient had enough medication available for use as directed. From this we calculated the number and percent of days covered by antihypertensive therapy for each patient throughout the full year following the index prescription, as we have described in previous work.[3,33,34]

Other Covariates

In addition to the assessments of psychosocial and behavioral variables described above, the patient survey also captured information about demographic, clinical, and health utilization characteristics, including: age, gender, marital status, race/ethnicity, primary language, living arrangements, level of education, and occupation; comorbid cardiovascular conditions; all currently used medications, perceptions of medication effectiveness and side effects, self-reported compliance, and measures taken to improve compliance. The medical records of participating subjects from 1996 were also reviewed and abstracted by research assistants. Information recorded from patients' charts included the presence of any diagnoses of depression.

Analyses

The proportion of days in the study year covered by antihypertensive medication was not normally distributed among survey respondents (Wilkes-Shapiro statistic 0.846; P = .0001). Therefore, the distribution of percent of days covered was divided using 2 cut points corresponding to 80% and 50% of days covered, thresholds that by convention are often used in studies of compliance.[35,36] These cut points divided the study population into 3 roughly equal–sized groups (tertiles). Because of the non-normal distribution of percent of days covered by antihypertensive medications, we then used ordinal logistic regression to study the crude effects of psychosocial and behavioral characteristics on compliance. Each initially assessed a single psychosocial or behavioral variable and predicted the likelihood of being in a higher tertile of compliance (expressed as percent of days covered by a blood pressure medication).

We next constructed a multivariable ordinal logistic regression model to estimate the independent effects of psychosocial and behavioral variables. We included variables representing age, gender, race, education level, site of treatment, coronary artery disease, and thiazide use in all models. We then used a step-wise forward selection procedure to identify significant psychosocial and behavioral variables as well as additional demographic, clinical, and health care utilization variables.

In all models, psychosocial and behavioral variables were represented continuously after we observed generally monotonic relationships with compliance across categorical levels (e.g., tertiles) of these variables. We checked to see whether relationships between compliance and continuously represented variables deviated from linearity by forcing higher order variables (e.g., squared) into final models. In addition, we examined whether there were interactions between significant psychosocial predictors and other variables. We also investigated whether the relationship between significant psychosocial predictors and compliance was mediated by other psychosocial variables by examining the extent to which the odds ratios (ORs) for significant psychosocial predictors were changed when single potential mediating variables were either inserted or deleted from the final model. All models were constructed using the logistic procedure in SAS.[37] The assumption of proportional odds was evaluated for all ordinal logistic regression models with the score test χ^2 statistic.

RESULTS

The characteristics of the study population, stratified by study site, are presented in Table 1. A total of 496 patients treated for hypertension completed the telephone interview, 248 from the HMO and 248 from the VA setting. Most patients were ≥65, male, white, had a high school education or less, were retired, married, and not living

Table 1. Characteristics of the Study Population (N = 496) by Site

Characteristic	VAMC Patients, % (n = 248)	HMO Patients, % (n = 248)	P Value
Age			.046
<55	15.3	21.0	
55–64	23.0	20.5	
65–74	45.2	35.5	
75+	16.5	23.0	
Gender			.001
Female	4.0	61.3	
Male	96.0	38.7	
Race			.094
White	93.5	96.8	
Non-white	6.5	3.2	
Education			.001
<High school	10.1	15.3	
High school	41.9	54.0	
>High school	48.0	30.7	
Retired			.001
Yes	20.6	33.5	
No	79.4	66.5	
Married			.851
Yes	64.5	65.3	
No	35.5	34.7	
Living alone			.605
Yes	24.2	26.2	
No	75.8	73.8	
Number of hospitalizations			.001
0	59.7	75.0	
1+	40.3	25.0	
Depression diagnosis in chart			.233
Yes	11.7	8.5	
No	88.3	91.5	
Antihypertensive compliance			.101
≥80% of days covered	28.6	29.4	
79%–50% of days covered	31.1	38.7	
<50% of days covered	40.3	31.9	

alone. Approximately one third of patients had been hospitalized, and one in ten had a diagnosis of depression recorded in their medical charts. There was a narrower distribution of ages among VA than HMO patients. VA patients were also significantly more likely than HMO patients to be male, more highly educated, retired, and hospitalized. Over one third of patients did not have enough antihypertensive medication to cover 50% of the study year; another third had enough medication to cover only 79% to 50% of the study year; fewer than one third were covered for ≥80% of the study year. No significant crude difference in the percentage of days covered by antihypertensive medications was observed between the VA and HMO sites.

Table 2 presents the crude relationships between psychosocial variables and compliance, derived from univariate ordinal logistic regression models. In these unadjusted analyses, there were no statistically significant relationships with compliance for any of the psychosocial or behavioral variables studied.

However, after we controlled for the potential confounding effects of demographic variables (age, gender, race, education, employment status, treatment site), use of thiazide diuretics, the presence of comorbid conditions (coronary artery disease, cerebrovascular disease, and renal failure), and locus of control, we found that an increase in depression symptom severity was significantly associated with a lower odds of compliance (adjusted OR of good compliance per point increase in the 14-point depression score, 0.93; 95% confidence interval [95% CI], 0.87 to 0.99; see Table 3). The magnitude and significance of this effect was not attributable to the addition of any single confounder to the model, but rather to the combination of all other included study variables.

When higher-order terms of depression severity score (i.e., squared, or squared as well as cubed) were forced into the final model, these terms were found to be statistically nonsignificant. When potential mediating psychosocial and behavioral variables were singly added to or subtracted from the final model, no change had an appreciable effect on the odds ratio for depression severity. For example, subtraction of the external locus of control score caused the odds ratio for depression severity to increase by only 1.6%; addition of satisfaction, social desirability, smoking status, social support, health beliefs, knowledge, or number of drinks had even less impact on the odds ratio for depression severity (0.5%, 0.1%, 0.1%, 0.1%, −0.1%, 0.1%, and 0.0% change, respectively). No significant interaction was found between depression severity and other demographic, clinical, or health care utilization variables.

In our adjusted analyses, we also observed a trend toward improved compliance with each point increase in the measure of external locus of control (adjusted OR per point increase, 1.14; 95% CI, 0.99 to 1.33; see Table 3). That is, patients who believed that events were determined by forces outside of themselves were more likely to take their antihypertensive medications as directed. The assumption of proportional odds was evaluated for the final ordinal logistic regression model and was found to be met (score test χ^2, with 11 *df*, 8.84; *P* = .90).

Because some earlier investigations have suggested a possible link between use of β-blockers[38] and depression, we examined whether depression symptom severity differed by antihypertensive drug class (i.e., ACE inhibitors, β-blockers, calcium channel blockers, thiazides, or other agents), and found no significant differences. Finally, in our analysis of the criterion validity of our adapted depression severity score, we found a statistically significant relationship between possessing a higher tertile of depression severity score and having a diagnosis of depression recorded in one's medical record (χ^2 test for trend, 2 *df*, 34.7; *P* ≤ .001).

DISCUSSION

To our knowledge, this is the first report of an association between depressive symptoms and poor

Table 2. Crude Odds Ratios Between Psychosocial/Behavioral Characteristics and Compliance with Blood Pressure Medications (*N* = 496)

Characteristic*	Crude OR*	95% CI
Depressive symptom severity (per 1-point increase)	0.97	0.91 to 1.03
External locus of control (per 1-point increase)	1.02	0.90 to 1.17
Satisfaction with medical care (per 1-point increase)	1.04	0.95 to 1.14
Knowledge regarding hypertension and its treatment (per 1-point increase)	1.03	0.94 to 1.12
Belief in the importance of hypertension treatment (per 1-point increase)	1.02	0.84 to 1.24
Social support regarding hypertension treatment (per 1-point increase)	0.93	0.71 to 1.21
Socially desirable responding (per 1-point increase)	1.02	0.94 to 1.11
Number of drinks per day (per 1-drink/day increase)	0.98	0.80 to 1.20
Smoker (compared to non-smokers)	0.90	0.56 to 1.45
Depression diagnosis in medical records	0.77	0.44 to 1.34

* From ordinal logistic regression models predicting the likelihood of being in a higher tertile of percent of the year covered by antihypertensive medications, considering single psychosocial/behavioral variables.
OR, odds ratio; CI, confidence interval.

Table 3. Independent Psychosocial Predictors of Compliance (*N* = 496)

Characteristic	Adjusted OR*	95% CI	*P* Value
Depression symptom severity (per 1-point increase)	0.93	0.87 to 0.99	.027
External locus of control (per 1-point increase)	1.15	0.99 to 1.33	.068

* *From an ordinal logistic regression model predicting the likelihood of being in a higher tertile of percent of the year covered by antihypertensive medications, controlling for demographic variables (age, gender, race, education level, employment status), site of treatment, use of thiazide diuretics, and the presence of comorbid conditions (coronary artery disease, cerebrovascular disease, and renal failure).*
OR, odds ratio; CI, confidence interval.

compliance with antihypertensive medications. Strengths of this study include the fact that we used actual drug utilization data rather than patient recall of adherence. Objective measures of compliance are especially important in investigations of depression because "pessimism bias" can cause under-reporting of drug use among the more severely depressed.[39] In addition, we adjusted for a wide range of other determinants of compliance, including sociodemographic, clinical, and health care utilization variables. As demonstrated in this study, unadjusted confounding can obscure the true effects of psychosocial variables such as depression by weakening both the strength and statistical significance of their apparent associations with noncompliance.

Depression has also been reported to have an effect on adherence to other primary and secondary prevention treatments. In one study of compliance with aspirin among elderly patients with coronary artery disease, depressed patients adhered to their regimen on a significantly lower proportion of days (45%) than those without depression (69%).[27] Studies of compliance in a variety of other conditions, including AIDS,[40] renal transplantation,[41] and asthma,[42] have also identified depression as a risk factor for nonadherence.

The precise mechanism by which depressive symptoms can affect compliance is not clear and may be quite complex. Several features of depression could have detrimental effects on adherence with preventive medications, including poor motivation, pessimism over the effectiveness of treatments, decrements in attention, memory, and cognition, decreased self-care, and even intentional self harm.[22,43–45] In addition, depression has been associated with greater sensitivity to unpleasant side effects from medications.[46] We did not find evidence that other psychosocial and behavioral variables play a mediating role.

Among the other psychosocial and behavioral factors studied, we observed a trend toward increased compliance with external rather than internal locus of control. The effect of this variable on compliance in prior investigations has been mixed.[25,47] One mechanism that could explain our observation is that patients who believe that their fate is determined by forces outside themselves may be more likely to take medications on the instructions of their physician.[48]

Some of the most interesting findings in relation to clinical practice are the psychosocial variables, which appeared to have no association with patient compliance. We did not observe significant independent effects on compliance for health beliefs or knowledge regarding hypertension and its treatment. Prior studies of the effects of these psychosocial variables have produced mixed results, and some investigators have suggested that their predictive value may be best for compliance with short-term (e.g., several weeks) rather than long-term treatments.[17] We also found no independent effects for social supports or patient satisfaction with health care. Previous studies have also failed to identify effects for these variables on adherence to antihypertensive medications.[21,30,49] The two health-related behaviors studied, alcohol consumption and tobacco use, also were not found to be related to compliance with antihypertensive medications; similar findings have been reported elsewhere.[26] These negative findings, too, have interesting clinical implications. They underscore the fact that clinicians cannot assume that any set of psychosocial characteristics are predictive of good or bad compliance. With the possible exception of those who are depressed, each patient must be considered to be equally at risk of being noncompliant, and evaluated with this possibility in mind.

Results of this study should be interpreted in light of some potential limitations. First, by using a measure of compliance based on filled prescriptions, we may have misclassified some compliant patients as noncompliant, such as those who obtained free samples from their doctors, were hospitalized for extended periods, or achieved blood pressure control through diet changes or exercise and were taken off antihypertensive medications. On the other hand, by using filled prescriptions to identify participants, we may have missed the most noncompliant patients, who did not fill any antihypertensive prescription in the study year. In addition, although our definition of noncompliance based on filled prescriptions measured medication underuse, it did not capture other types of noncompliance, such as overuse or inappropriate timing of dosages.

Second, we did not formally evaluate the reliability and validity of many of our adapted psychosocial and behavioral scales. However, in a post hoc analysis of the criterion validity of our adapted depression severity scale, we did find that depression symptom severity scores were significantly related to having a diagnosis of depression recorded in one's medical record. Third, potential limitations may have been

introduced by the high nonresponse rate in our study. For example, if nonrespondents had worse compliance than respondents, our observed levels of compliance would have been inflated and the generalizability of our findings would have been limited. Finally, we cannot exclude the possibility that the variables found to be associated with compliance were not a result of multiple comparisons made using a number of candidate variables.

If confirmed in future studies, these findings regarding the relationship between depressive symptoms and anti-hypertensive medication compliance may have important implications for both researchers and clinicians. First, they may help to explain the higher cardiovascular morbidity and mortality that have been repeatedly observed in depressed patients.[50–54] Second, these data suggest that patients with depressive symptoms should have their adherence to antihypertensive medications monitored particularly closely and may require special encouragement from health care providers in this regard. Finally, these data provide additional impetus for improving the detection and treatment of mental health problems. Although the majority of patients with depression present in primary care, there is substantial evidence that depression is underdetected and inadequately treated in such settings.[55–57] Increased efforts to detect and treat depression may be associated with additional health benefits due to better blood pressure control. In the future, intervention trials might be conducted to clarify whether treatment of depression in noncompliant patients results in improvement in their adherence to prescribed regimens. Several initial studies in this area have yielded some promising findings.[58–60]

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